

FIGURE 1

Murine Antibody 3B9 Light Chain
Native Signal Sequence and Variable Region

Nucleotide Sequence SEQ ID NO:1

Amino Acid Sequence SEQ ID NO:2

ATG GAG ACA GAC ACA ATC CTG CTA TGG GTG CTG CTG CTC	39
Met Glu Thr Asp Thr Ile Leu Leu Trp Val Leu Leu Leu	
1 5 10	
TGG GTT CCA GGC TCC ACT GGT GAC ATT GTG CTG ACC CAA	78
Trp Val Pro Gly Ser Thr Gly Asp Ile Val Leu Thr Gln	
15 20 25	
TCT CCA GCT TCT TTG GCT GTG TCT CTA GGG CAG AGG GCC	117
Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala	
30 35	
ACC ATC TCC TGC AAG GCC AGC CAA AGT GTT GAT TAT GAT	156
Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp	
40 45 50	
GGT GAT AGT TAT ATG AAC TGG TAC CAA CAG AAA CCA GGA	195
Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly	
55 60 65	
CAG CCA CCC AAA CTC CTC ATC TAT GCT GCA TCC AAT CTA	234
Gln Pro Pro Lys Leu Leu Ile Tyr Ala Ala Ser Asn Leu	
70 75	
GAA TCT GGG ATC CCA GCC AGG TTT AGT GGC AGT GGG TCT	273
Glu Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser	
80 85 90	
GGG ACA GAC TTC ACC CTC AAC ATC CAT CCT GTG GAG GAG	312
Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Glu	
95 100	
GAG GAT GCT GCA ACC TAT TAC TGT CAG CAA AGT AAT GAG	351
Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Ser Asn Glu	
105 110 115	
GAT CCT CCG ACG TTC GGT GGA GGC ACC AAG CTG GAA ATC	390
Asp Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile	
120 125 130	
AAA CGG	396
Lys Arg	

Figure 2

Murine Antibody 1B9 Heavy Chain
Native Signal Sequence and Variable Region

Nucleotide Sequence SEQ ID NO: 3

Amino Acid Sequence SEQ ID NO: 4

GAATTCGCGG CCGCTATGCA GGGACAATCA GCAGCAGCAA	40
TGAGGAAGTA AGCCTGTGCA GAT ATG AAC AGG CTT ACT TCC	81
Met Asn Arg Leu Thr Ser	
1 5	
TCA TTG CTG CTG CTG ATT GTC CCT GCA TAT GTC CTG TCC	120
Ser Leu Leu Leu Leu Ile Val Pro Ala Tyr Val Leu Ser	
10 15	
CAG GTT ACT CTG AAA GAG TCT GGC CCT GGG ATA TTG CAG	159
Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln	
20 25 30	
CCC TCC CAG ACC CTC AGT CTG ACT TGT TCT TTC TCT GGG	198
Pro Ser Gln Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly	
35 40 45	
TTT TCA CTG AGC ACT TCT GGT ATG GGT GTG AGC TGG ATT	237
Phe Ser Leu Ser Thr Ser Gly Met Gly Val Ser Trp Ile	
50 55	
CGT CAG CCT TCA GGA AAG GGT CTG GAG TGG CTG GCA CAC	276
Arg Gln Pro Ser Gly Lys Gly Leu Glu Trp Leu Ala His	
60 65 70	
ATT TAC TGG GAT GAT GAC AAG CGC TAT AAC CCA TCC CTG	315
Ile Tyr Trp Asp Asp Asp Lys Arg Tyr Asn Pro Ser Leu	
75 80	
AAG AGC CGG CTC ACA ATC TCC AAG GAT ACC TCC AGC AAC	354
Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Ser Asn	
85 90 95	
CAG GTA TTC CTC AAG ATC ACC AGT GTG GAC ACT GCA GAT	393
Gln Val Phe Leu Lys Ile Thr Ser Val Asp Thr Ala Asp	
100 105 110	
ACT GCC ACA TAC TAC TGT GCT CGA AGA GAG ACT GTG TTC	432
Thr Ala Thr Tyr Tyr Cys Ala Arg Arg Glu Thr Val Phe	
115 120	

Figure 2 (con't)

TAC	TGG	TAC	TTC	GAT	GTC	TGG	GGC	GCA	GGG	ACC	ACG	GTC	471
<u>Tyr</u>	<u>Trp</u>	<u>Tyr</u>	<u>Phe</u>	<u>Asp</u>	<u>Val</u>	Trp	Gly	Ala	Gly	Thr	Thr	Val	
125						130					135		
ACC	GTC	TCC	TCA										483
Thr	Val	Ser	Ser										
			140										

FIGURE 3

Human/Murine 3B9 Chimeric Antibody Heavy Chain
Signal Sequence and Variable Region

Nucleotide Sequence SEQ ID NO: 9

Amino Acid Sequence SEQ ID NO:10

ATG GTG TTG CAG ACC CAG GTC TTC ATT TCT CTG TTG CTC	39
Met Val Leu Gln Thr Gln Val Phe Ile Ser Leu Leu Leu	
1 5 10	
TGG ATC TCT GGT GCC TAC GGG CAG GTT ACC CTG AAA GAG	78
Trp Ile Ser Gly Ala Tyr Gly Gln Val Thr Leu Lys Glu	
15 20 25	
TCT GGC CCT GGG ATA TTG CAG CCC TCC CAG ACC CTC AGT	117
Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln Thr Leu Ser	
30 35	
CTG ACT TGT TCT TTC TCT GGG TTT TCA CTG AGC ACT TCT	156
Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser <u>Thr Ser</u>	
40 45 50	
GGT ATG GGT GTG AGC TGG ATT CGT CAG CCT TCA GGA AAG	195
<u>Gly Met Gly Val Ser</u> Trp Ile Arg Gln Pro Ser Gly Lys	
55 60 65	
GGT CTG GAG TGG CTG GCA CAC ATT TAC TGG GAT GAT GAC	234
Gly Leu Glu Trp Leu Ala <u>His Ile Tyr Trp Asp Asp Asp</u>	
70 75	
AAG CGC TAT AAC CCA TCC CTG AAG AGC CGG CTC ACA ATC	273
<u>Lys Arg Tyr Asn Pro Ser Leu Lys Ser</u> Arg Leu Thr Ile	
80 85 90	
TCC AAG GAT ACC TCC AGC AAC CAG GTA TTC CTC AAG ATC	312
Ser Lys Asp Thr Ser Ser Asn Gln Val Phe Leu Lys Ile	
95 100	
ACC AGT GTG GAC ACT GCA GAT ACT GCC ACA TAC TAC TGT	351
Thr Ser Val Asp Thr Ala Asp Thr Ala Thr Tyr Tyr Cys	
105 110 115	
GCT CGA AGA GAG ACT GTG TTC TAC TGG TAC TTC GAT GTC	390
Ala Arg <u>Arg Glu Thr Val Phe Tyr Trp Tyr Phe Asp Val</u>	
120 125 130	
TGG GGC GCA GGG ACC ACG GTC ACC GTC TCC TCA	423
Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser	
135 140	

4/11

SUBSTITUTE SHEET (RULE 26)

0989461-061201

FIGURE 4

Humanized 3B9 Antibody Heavy Chain
Signal Sequence and Variable Region

Nucleotide Sequence SEQ ID NO: 11

Amino Acid Sequence SEQ ID NO: 12

ATG GTG TTG CAG ACC CAG GTC TTC ATT TCT CTG TTG CTC	39
Met Val Leu Gln Thr Gln Val Phe Ile Ser Leu Leu Leu	
1 5 10	
TGG ATC TCT GGT GCC TAC GGG CAG GTT ACC CTG CGT GAA	78
Trp Ile Ser Gly Ala Tyr Gly Gln Val Thr Leu Arg Glu	
15 20 25	
TCC GGT CCG GCA CTA GTT AAA CCG ACC CAG ACC CTG ACG	117
Ser Gly Pro Ala Leu Val Lys Pro Thr Gln Thr Leu Thr	
30 35	
TTA ACC TGC ACC TTC TCC GGT TTC TCC CTG TCG ACC TCC	156
Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser <u>Thr Ser</u>	
40 45 50	
GGT ATG GGT GTT TCC TGG ATC CGT CAG CCG CCG GGT AAA	195
<u>Gly Met Gly Val Ser</u> Trp Ile Arg Gln Pro Pro Gly Lys	
55 60 65	
GGT CTA GAA TGG CTG GCT CAC ATC TAC TGG GAC GAC GAC	234
Gly Leu Glu Trp Leu Ala <u>His Ile Tyr Trp Asp Asp Asp</u>	
70 75	
AAA CGT TAC AAC CCG AGC CTG AAA TCC CGT CTG ACG ATA	273
<u>Lys Arg Tyr Asn Pro Ser Leu Lys Ser</u> Arg Leu Thr Ile	
80 85 90	
TCC AAA GAC ACC TCC CGT AAC CAG GTT GTT CTG ACC ATG	312
Ser Lys Asp Thr Ser Arg Asn Gln Val Val Leu Thr Met	
95 100	
ACT AAC ATG GAC CCG GTT GAC ACC GCT ACC TAC TAC TGC	351
Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr Cys	
105 110 115	
GCT CGA CGC GAA ACC GTT TTC TAC TGG TAC TTC GAC GTT	390
Ala Arg <u>Arg Glu Thr Val Phe Tyr Trp Tyr Phe Asp Val</u>	
120 125 130	
TGG GGT CGT GGT ACC CCA GTT ACC GTG AGC TCA	423
Trp Gly Arg Gly Thr Pro Val Thr Val Ser Ser	
135 140	

FIGURE 5

Humanized 3B9 Antibody Light Chain
Signal Sequence and Variable Region

Nucleotide Sequence SEQ ID NO: 13

Amino Acid Sequence SEQ ID NO: 14

ATG GGA TGG AGC TGT ATC ATC CTC TTC TTG GTA GCA ACA	39
Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr	
1 5 10	
GCT ACA GGT GTC CAC TCC GAT ATC GTG ATG ACC CAG TCT	78
Ala Thr Gly Val His Ser Asp Ile Val Met Thr Gln Ser	
15 20 25	
CCA GAC TCG CTA GCT GTG TCT CTG GGC GAG AGG GCC ACC	117
Pro Asp Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr	
30 35	
ATC AAC TGC AAG GCC TCC CAA AGT GTT GAT TAT GAT GGT	156
Ile Asn Cys <u>Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly</u>	
40 45 50	
GAT AGT TAT ATG AAC TGG TAT CAG CAG AAA CCC GGG CAG	195
<u>Asp Ser Tyr Met Asn</u> Trp Tyr Gln Gln Lys Pro Gly Gln	
55 60 65	
CCT CCT AAG TTG CTC ATT TAC GCT GCA TCC AAT CTA GAA	234
Pro Pro Lys Leu Leu Ile Tyr <u>Ala Ala Ser Asn Leu Glu</u>	
70 75	
TCT GGG GTA CCT GAC CGA TTC AGT GGC AGC GGG TCT GGG	273
<u>Ser</u> Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly	
80 85 90	
ACA GAT TTC ACT CTC ACC ATC AGC AGC CTG CAG GCT GAA	312
Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu	
95 100	
GAT GTG GCA GTA TAC TAC TGT CAG CAA AGT AAT GAG GAT	351
Asp Val Ala Val Tyr Tyr Cys <u>Gln Gln Ser Asn Glu Asp</u>	
105 110 115	
CCT CCG AGG TTC GGC GGA GGG ACC AAG GTG GAG ATC AAA	390
<u>Pro Pro Arg</u> Phe Gly Gly Gly Thr Lys Val Glu Ile Lys	
120 125 130	
CGT	393
Arg	

FIGURE 6A

Signal Sequence

Nucleotide SEQ ID NO:5

Amino Acid SEQ ID NO:6

ATG	GTG	TTG	CAG	ACC	CAG	GTC	TTC	ATT	TCT	CTG	TTG	CTC	39
Met	Val	Leu	Gln	Thr	Gln	Val	Phe	Ile	Ser	Leu	Leu	Leu	
1				5					10				

TGG	ATC	TCT	GGT	GCC	TAC								
Trp	Ile	Ser	Gly	Ala	Tyr								
	15												

FIGURE 6B

Signal Sequence

Nucleotide SEQ ID NO:7

Amino Acid SEQ ID NO:8

ATG	GGA	TGG	AGC	TGT	ATC	ATC	CTC	TTC	TTG	GTA	GCA	ACA	39
Met	Gly	Trp	Ser	Cys	Ile	Ile	Leu	Phe	Leu	Val	Ala	Thr	
1				5					10				

GCT	ACA	GGT	GTC	CAC	TCC	GAT	ATC	GTG	ATG	ACC	CAG	TCT	78
Ala	Thr	Gly	Val	His	Ser	Asp							
	15					20							

SUBSTITUTE SHEET (RULE 26)

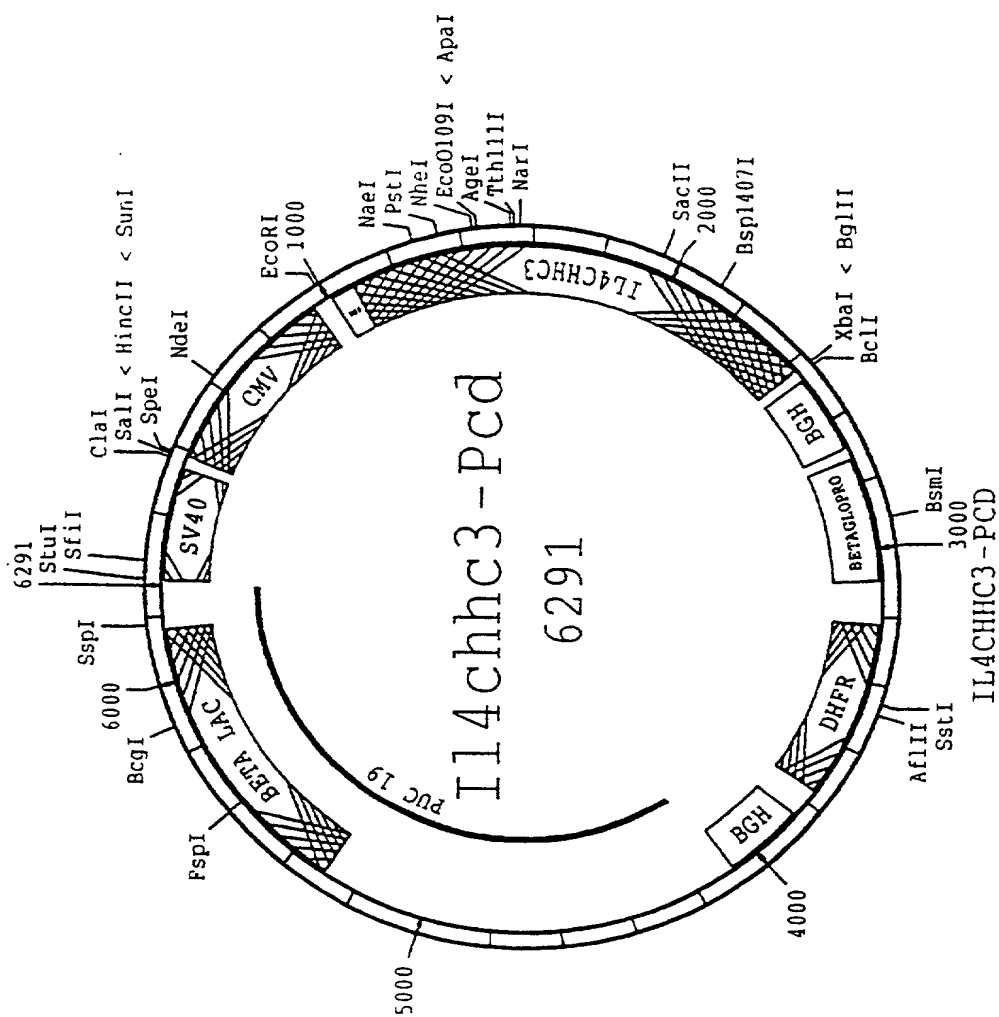


FIGURE 8

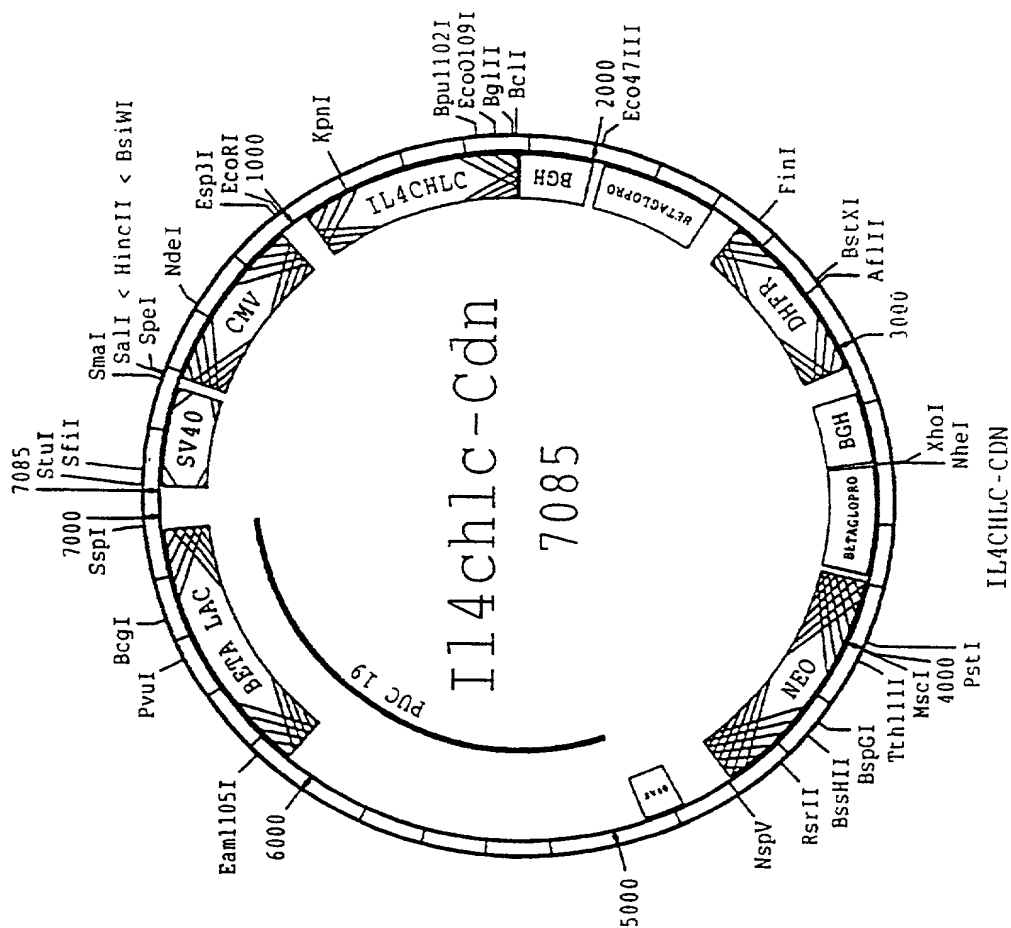
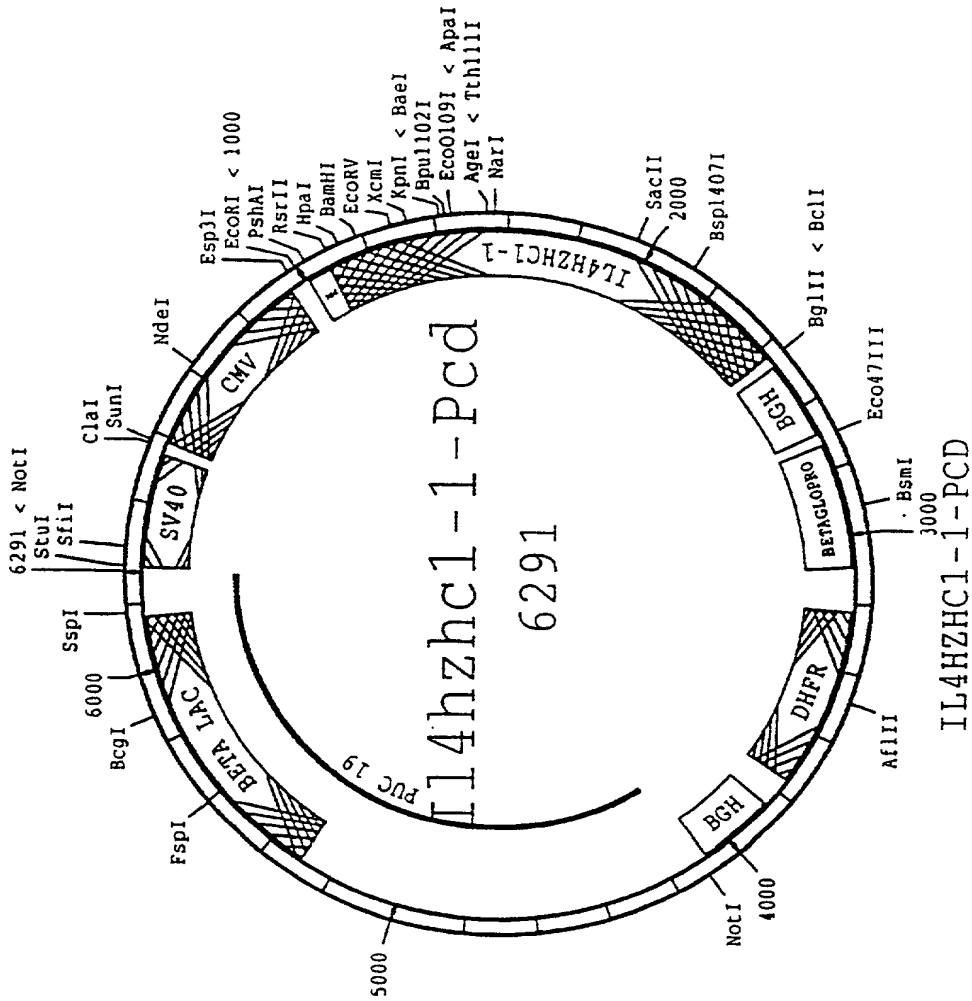


FIGURE 9



102790" 19462860

FIGURE 10

